REMARKS

No new matter has been added. The Applicants again request entry of the amendments as set forth in the Appendices hereto prior to examination of the application on the merits.

Respectfully submitted,

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Enclosure: Version with Markings Showing Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please replace paragraph **[0018]** with the following:

[0018] As an example of a known partial rebreathing process, the NICO™ system offered by Novametrix Medical Systems Inc. of Wallingford, Connecticut, employs a 60 second baseline period, a 50 second rebreathing period, and a 70 second recovery period. The complete rebreathing cycle lasts for about three minutes. Another exemplary partial rebreathing process is disclosed in Capek, JM, and Roy, RJ, Noninvasive measurement of cardiac output using partial CO_2 rebreathing, IEEE Trans Biomed Eng 1988; 35:653-661. That rebreathing process has a total cycle time of about 3½ minutes, with the actual rebreathing phase lasting for about 30 seconds. Gama de Abreu, M, et al., Partial carbon dioxide rebreathing: A reliable technique for noninvasive measurement of nonshunted pulmonary capillary blood flow, Crit. Care Med. 1997; 25: 675-683, discloses a rebreathing process with a 35 second rebreathing phase and a total cycle time, including baseline and recovery phases, of about 3 minutes.

Please replace paragraph **[0067]** with the following:

[0067] Since $CvCO_2$ may change over time, an accurate [non-invasive] noninvasive Fick-based determination of the pulmonary capillary blood flow or cardiac output of a patient may include an estimation of the rate at which $CvCO_2$ changes. With an exemplary assumption that changes in $CvCO_2$ are substantially linear over the rebreathing cycle and, therefore, that the rate of change is constant, the rate of change in $CvCO_2$, represented as "k", may be determined with the following equation:

$$k = \frac{\Delta CvCO_2}{\Delta t}. \qquad (10)$$

Alternatively, the change in carbon dioxide content of the venous blood may be assumed to substantially follow a curve of some other shape that is reasonably based on the character of the change in carbon dioxide content, such as an exponential curve, wherein the rate of change would also be exponential, or the curve of a polynomial. As another alternative, the rate of

change in $CvCO_2$ may be approximated by an artificial neural network or a radial basis function, as known in the art.

Please replace paragraph **[0082]** with the following:

[0082] The $PetCO_2$ of the patient is also measured for each of the "before", "during" and "after" phases. As $PetCO_2$, when corrected for parallel deadspace (of [non-perfused] nonperfused alveoli), is assumed to be equal to the partial pressure of carbon dioxide in the alveolar blood (P_ACO_2) and the partial pressure of CO_2 in the arterial blood ($PaCO_2$), a carbon dioxide dissociation curve may be employed with the end tidal carbon dioxide partial pressure measurements, as known in the art, to determine the content of carbon dioxide in blood of the alveoli (C_ACO_2) of the lungs of the patient that participate in the exchange of blood gases, which alveoli are typically referred to as "perfused" alveoli, for each of the before, during, and after rebreathing phases. C_ACO_2 is assumed to be equal to the content of carbon dioxide in the arterial blood ($CaCO_2$). FIG. 4 is a graph that illustrates the $PetCO_2$ measured during each of the before, during, and after phases of the rebreathing process of the present invention.

Please replace paragraph **[0110]** with the following:

[0110] Another exemplary method for modifying data in the [best fit] best-fit line method is depicted in FIGs. 8A and 8B. As with the filtering and clustering methods for modifying data, the method depicted in FIGs. 8A and 8B includes selection of data points that are most likely to facilitate an accurate determination of the location and orientation of a best-fit line and, thus, of the pulmonary capillary blood flow or cardiac output of a patient. This method for modifying data includes iteratively examining data points and the distribution of the remaining data points relative to the two lines representing the range of possible pulmonary capillary blood flow measurements.

Please replace paragraph **[0112]** with the following:

[0112] Next, the number of other data points 130 located between lines 110 and 120 is determined. If the number of data points 130 between lines 110 and 120 is equal to or exceeds a threshold number, the analyzed data point 130 is retained for a subsequent determination of the location and orientation of a best-fit line through the data. Otherwise, the analyzed data point 130 is discarded. The threshold number of data points that must be located between line 110 and line 120 for an analyzed data point to be retained may be a predetermined value or determined by other means. As <u>an</u> example, the threshold number may be set to the median number of data points that are located between line 110 and line 120 when each data point 130 of a set of data points 130 has been evaluated in accordance with the present embodiment of the method for modifying data. This process is repeated until each data point 130 in a set of data points 130 has been so evaluated. FIG. 8A depicts use of the data modification method on a data point 130 that will be retained, while FIG. 8B illustrates use of the present embodiment of the data modification method on another data point 130′ that will not be retained.

Please replace paragraph **[0121]** with the following:

[0121] The relatively short phases of differential Fick techniques incorporating teachings of the present invention, as well as the lack of a recovery or stabilization period, facilitate the calculation and, thus, reporting of noninvasive pulmonary capillary blood flow or cardiac output measurements with increased frequency over that possible with previously known differential Fick techniques. For example, when conventional partial rebreathing techniques are employed, pulmonary capillary blood flow and cardiac output values can only be updated as frequently as the cycle time for these methods, which is typically three minutes or longer. In contrast, when the differential Fick method of the present invention is embodied as a partial rebreathing process with rebreathing and [non-rebreathing] <u>nonrebreathing</u> phases that last about thirty seconds, the pulmonary capillary blood flow and cardiac output of a patient can be updated following the completion of each phase, or about every thirty seconds.

Please replace the Abstract on page 51 with the following:

A differential Fick technique including a first phase in which baseline breathing parameters may be established and a second phase in which a change in the effective ventilation of a patient is induced. The durations of the first and second phases may be substantially the same[,] and may be abbreviated relative to the durations of comparable phases of previously known differential Fick techniques. The disclosed differential Fick technique also lacks a recovery period in which the respiratory parameters of a patient are permitted to return to "normal" levels.

IN THE CLAIMS

1. (Amended) A rebreathing method, consisting essentially of:
effecting a [non-rebreathing] nonrebreathing period; and
effecting a rebreathing period, said rebreathing period having substantially a same duration as said [non-rebreathing] nonrebreathing period.

2. (Amended) The rebreathing method of claim 1, wherein said [non-rebreathing] nonrebreathing period and said rebreathing period are each effected for about 30 seconds.

3. (Amended) The rebreathing method of claim 1, wherein said [non-rebreathing] nonrebreathing period is effected for a duration of at least about 30% of a combined duration of said [non-rebreathing] nonrebreathing period and said rebreathing period.

4. (Amended) The rebreathing method of claim 1, wherein said rebreathing period is effected for a duration of at least about 30% of a combined duration of said [non-rebreathing] nonrebreathing period and said rebreathing period.

5. (Amended) The rebreathing method of claim 1, further comprising repeating said [non-rebreathing] nonrebreathing period and said rebreathing period in sequence.

6. (Amended) The rebreathing method of claim 1, further comprising effecting said [non-rebreathing] nonrebreathing period and said rebreathing period for a combined duration of at most about 2 minutes.

7. (Amended) The rebreathing method of claim 1, further comprising optimizing a duration of at least one of said rebreathing period and said [non-rebreathing] nonrebreathing period.

8. (Amended) The rebreathing method of claim 1, wherein said effecting said [non-rebreathing] nonrebreathing period includes obtaining respiratory measurements prior to said effecting said rebreathing period.

9. (Amended) The rebreathing method of claim 1, wherein a transition between said effecting said [non-rebreathing] nonrebreathing period and said effecting said rebreathing period is gradual.

10. (Amended) The rebreathing method of claim 1, further comprising optimizing durations of said [non-rebreathing] nonrebreathing period and said rebreathing period.

13. (Amended) A rebreathing method comprising:

causing a patient to inhale gas or a gas mixture comprising an increased [concentration] amount of carbon dioxide for a rebreathing period of time;

causing the patient to inhale another gas or gas mixture comprising at least [a concentration] an amount of oxygen present in air for a [non-rebreathing] nonrebreathing period of time, said rebreathing period of time and said [non-rebreathing] nonrebreathing period of time being substantially the same.

14. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] amount of carbon dioxide and said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] amount of oxygen present in air are effected in immediate succession.

15. (Amended) The rebreathing method of claim 13, further comprising repeating said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] amount of carbon dioxide and said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] amount of oxygen present in air in sequence.

17. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air is effected for a [non-rebreathing] <u>nonrebreathing</u> period of about 30 seconds.

18. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] <u>amount</u> of carbon dioxide is effected for a rebreathing time period comprising at least about 30% of a combined duration of said rebreathing period of time and said [non-rebreathing] <u>nonrebreathing</u> period of time.

19. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said another gas or gas mixture comprising at least said amount of oxygen present in air is effected for a [non-breathing] <u>nonrebreathing</u> [time period] <u>period of time</u> comprising at least about 30% of a combined duration of said rebreathing period of time and said [non-breathing] <u>nonrebreathing</u> [time period] <u>period of time</u>.

22. (Amended) The rebreathing method of claim 21, wherein said [effect] <u>effecting</u> said partial rebreathing comprises bi-directional rebreathing.

24. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air comprises permitting the patient to inhale air.

25. (Amended) The rebreathing method of claim 13, wherein at least one of said causing the patient to inhale gas or a gas mixture comprising an increased [concentration] <u>amount</u> of carbon dioxide and said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air comprises assisting the patient's breathing with a ventilator.

26. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] <u>amount</u> of carbon dioxide and said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air are effected for a combined cycle period of at most about 2 minutes.

27. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air immediately follows said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] <u>amount</u> of carbon dioxide and is immediately followed by again causing the patient to inhale a gas or a gas mixture comprising an increased amount of carbon dioxide.

28. (Amended) The rebreathing method of claim 13, further comprising optimizing a duration of at least one of said causing the patient to inhale said gas or said gas mixture comprising said increased [concentration] <u>amount</u> of carbon dioxide and said causing the patient to inhale said another gas or gas mixture comprising at least said [concentration] <u>amount</u> of oxygen present in air.

29. (Amended) The rebreathing method of claim 13, wherein said causing the patient to inhale another gas or gas mixture comprising at least [a concentration] <u>an amount</u> of oxygen present in air for [a] <u>said</u> [non-rebreathing] <u>nonrebreathing</u> period of time is effected before initiation of rebreathing.

31. (Amended) The rebreathing method of claim 13, further comprising optimizing said rebreathing period of time and said [non-rebreathing] <u>nonrebreathing</u> period of time.

77. (Amended) The differential Fick technique of claim 70, wherein said first phase comprises a rebreathing phase and said second phase comprises a [non-rebreathing] nonrebreathing phase.

88. (Amended) The differential Fick technique of claim 84, wherein said first [period] duration of time of said inducing and said second [period] duration of time of said removing are substantially the same.

89. (Amended) The differential Fick technique of claim 88, wherein said first [period] duration of time of said inducing is at least about 30% of a combined duration of said first said [period] duration of time and said second [period] duration of time.

90. (Amended) The differential Fick technique of claim 88, wherein said second [period] duration of time of said removing is at least about 30% of a combined duration of said first [period] duration of time and said second [period] duration of time.

93. (Amended) The differential Fick technique of claim 84, wherein said inducing comprises causing the [patient] individual to rebreathe.

94. (Amended) The differential Fick technique of claim 84, wherein said obtaining measurements comprises obtaining measurements of carbon dioxide in respiration of the [patient] individual.

102. (Amended) The method of claim 101, wherein said obtaining measurements [comprising] comprises obtaining a measurement of at least carbon dioxide in respiration of the patient.

113. (Amended) The method of claim 110, wherein each of said evaluatings [comprising] <u>comprises</u> measuring at least one respiratory gas and respiratory flow of the patient.